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CLINICAL OUTCOMES STUDIES

Epidemiology and Disease Burden of Ulcerative Colitis in Taiwan: A Nationwide Population-Based Study

Chung-Yu Chen, MSc[1], Kun-Tai Lee, MD[2], Charles Tzu-Chi Lee PhD[3], Wen-Ter Lai, MD[4], Yaw-Bin Huang, PhD[5,6,]*

[1]*School of Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan;* [2]*Division of Cardiology, Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan;* [3]*Department of Public Health, Kaohsiung Medical University, Kaohsiung, Taiwan;* [4]*Department of Internal Medicine, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan;* [5]*Graduate Institute of Clinical Pharmacy, Kaohsiung Medical University, Kaohsiung, Taiwan;* [6]*Department of Pharmacy, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan*

ABSTRACT

Objectives: A rising trend of incidence and prevalence of ulcerative colitis (UC) had been noticed in Asian countries. We conducted this study to investigate the epidemiology and medical burden of UC in Taiwan. **Methods:** In this 10-year retrospective database study, we identified cases of patients with UC during 1998 to 2008 from the Taiwan National Health Insurance Research Database. Patients who had a catastrophic illness certificate were included in epidemiology and medical burden calculation. **Results:** There were 1522 cases identified in our study period. The incidence increased twofold from 0.37 per 100,000 in 1998 to 0.78 per 100,000 in 2008. The incidence and prevalence had an increasing trend in our population. The cases onset age was 45.0 years on average. In our survey, most of the top 20 coexisting diseases were gastrointestinally relevant diseases, anemia (9.99%), and hypertension (7.69%). There were more than 70% patients using mesalamine, and the medical expenditure on mesalamine occupied the highest position in patients with UC. The average medical expenditure of patients with UC had a decreasing trend after 2001. **Conclusions:** This study had the largest sample and the longest study period for the epidemiology and medical burden estimation of UC in Taiwan. The incidence rates and medicine use of patients with UC had a definite rising trend across the years in Taiwan. Patients with anemia or choric diseases were observed in our population. More surveillance of UC-related diseases and health care costs need to be conducted in the future.

Keywords: disease burden, epidemiology, medical expenditures, ulcerative colitis.

Introduction

Ulcerative colitis (UC) is a rare idiopathic inflammatory disease of the colon and the rectum that makes the estimation of incidence and prevalence rates difficult in Asians. A number of studies have shown that the prevalence and incidence of UC are increasing in Asians, especially in East Asian countries, including Hong Kong, Korea, and Japan [1–5], although the exact etiology and mechanisms for this trend are not clear [6–8]. Multiple factors may be involved, including lifestyle [9,10], environment factors [11], genetics [12–17], gender, and the immunological system [18,19]. Upon reviewing previous research, we found that only one study had reported the prevalence rates of UC by using data from a tertiary referral center in Taiwan [20]. As a result, the current report on UC epidemiologic outcome in Taiwan was limited [21–24].

Furthermore, a number of studies noted that the clinical features and natural history of Asian patients with UC may be different from those of Western patients, including extent of disease, relapse rate, incidence of colorectal cancer (CRC), and mortality [7,25,26]. The symptoms and signs of UC include distal colitis, extensive colitis, diarrhea mixed with blood and mucus, constipation, weight loss, crampy pain, abdominal pain, low-grade fever, and anemia [27,28]. Moreover, a recent study showed that anemia is very common in inflammatory bowel disease and the prevalence in patients with inflammatory bowel disease ranged from 9% to 74% [29]. UC can also be associated with local and extraintestinal complications. There are some severe local complications of UC, including fulminant colitis, intestinal perforation and stricture, massive hemorrhage, and the development of CRC [2,30]. A numbers of studies have also indicated that UC may be associated with a number of extraintestinal complication, including iritis, arthritis, panniculitis, and deep venous thrombosis [31–33]. Therefore, appropriate diagnosis and treatment are important in UC. In most cases of UC, the treatment goals are prolonging remission, decreasing prognosis of disease severity, and increasing quality of life as previous reports have shown that patients with UC are associated with decreasing

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* *Address correspondence to:* Yaw-Bin Huang, No. 100, Shihcyuan 1st Road, Sanmin District, Kaohsiung City 80708, Taiwan, R.O.C.
E-mail: yabihu@kmu.edu.tw.

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quality of life and high morbidity [34–36]. The published literature on the economic burden of patients with UC is currently limited. A previous report in the United States described the mean annual costs of $5066 for UC in 10,364 patients from year 2003 to 2004, with 73% of the costs being attributable to hospitalization and outpatient care and 27% to pharmaceutical claims [37]. Despite the study demonstrating the substantial economic burden of UC, the time trend of medical costs in managing patients with UC could not be observed in this study.

The aims of this study were 1) to investigative the incidence, prevalence, and coexisting diseases of UC in Taiwan, using a 10-year nationwide population-based database, and 2) to describe the distribution of drug utilization and medical expenditures of treatment of UC in Taiwan between inpatients and outpatients.

Methods

This is a population-based retrospective study for which data on patients with UC were extracted from the list of catastrophic illness (CI) certificates published during 1997 to 2008 by the Department of Health, Executive Yuan of Taiwan. UC cases were identified by using the *International Classification of Diseases, Ninth Revision* code 556. A UC diagnosis on a CI certificate needs to be strictly evaluated by at least two gastroenterologists according to the laboratory data and images from applied hospital (sigmoidoscopy and biopsies of the mucosa is the standard criterion used by the Taiwan government), and all documents are rechecked by a third physician in the Department of Health before a CI certificate is issued. Patients with CI certificates are eligible for exemption from insurance premiums and co-payments in National Health Insurance. The approval of the CI certificate needs strict evaluation by the Department of Health, and it may lead to underestimation of the actual number of cases. Although the actual number of cases may be underestimated, UC diagnosis and coding are accurate. We extracted the medical records of UC cases from the National Health Insurance Research Database (NHIRD). The National Health Research Institute provided the database, and the database includes information on outpatient, ambulatory, hospital inpatient care, dental services, and prescription drugs. Because this study was based in part on data from the NHIRD, which in this study consisted of de-identified secondary data released to the public for research purposes, this study was exempt from full review by the ethical committee, and informed consent did not need to be obtained from study subjects. In this study, subjects with UC CI certificates were included for the calculation of incidence and prevalence rates (1998–2008).

The following data were included for analysis: gender, onset of diagnosis age, and top 20 coexisting diseases after UC diagnosis. The new case numbers in each year were recorded to calculate the annual incidence rate from 1998 to 2008. The incidence rate for the CI certificates was calculated to track their first UC medical claim date. The prevalence rate for the CI certificates was also calculated to track their first yearly UC medical claim date.

For assessing time trend of medical costs in the treatment of patients with UC, we focused on drug utilization and medical expenditures in each year, and categorized medication into the following categories: 5-aminosalicylic acid derivate (including mesalamine and sulfasalazine, which were common use in Taiwan), corticosteroids, and immunosuppressant agents (azathioprine, cyclosporine, 6-mercatopurine, and Tacrolimus). Otherwise, each medical claim was classified as inpatient or outpatient. To compare the average medical expenditure in the treatment of patients with UC with that of the general Taiwan population in each year, we quote the average medical expenditure per UC patient fold to average expenditure on medicine per capita from National Health Expenditure, published by the Department of Health, Executive Yuan of Taiwan (http://www.doh.gov.tw/EN2006/DM/DM2.aspx?now_fod_list_no=12117&class_no=390&level_no=2).

Statistics

The crude incidence rate was calculated by using the total number of residents in each year from 1998 to 2008 as the denominator and the total number of new cases of patients with UC in each year as the numerator. The crude prevalence rate was calculated by using the total number of residents in each year as the denominator and the total number of cases of patients with UC in each year as the numerator. The incidence and prevalence rates were expressed as the number of cases per 100,000. We adjusted incidence and prevalence rates by age by using the standard population of the year 2000. Medical expenditure was calculated in each category (mesalamine, sulfasalazine, corticosteroids, and immunosuppressant agents) by outpatient, inpatient, and total medical claims each year. Average medical expenditure per patient with UC in each year from 1998 to 2008 was calculated by using all medical services expenditure in that year as the denominator and the total number of medical users in that year as the numerator. We also compared the average medical expenditure per UC patient fold to the average medical expenditure per capita in Taiwan from 1998 to 2008. All statistical analyses were carried out by using SAS 9.2.

Results

Among 10-year follow-up in Taiwan population, 1522 cases (945 males and 577 females) were identified. During 1998 to 2008, there were 1518 new cases. The 10-year average crude incidence rate was 0.66 patients with UC per 100,000 (Table 1). The crude incidence rate in 1998 was 0.37 per 100,000 and in 2008 was 0.78 per 100,000 in our population. The age-adjusted incidence rate in 1998 and 2008 was 0.38 and 0.72 per 100,000, respectively. Despite the fact that the incidence rate over the past decade had risen twofold from 1998 to 2008 in Taiwan, there was quite a lot of variation in the rate from year to year. The crude incidence rate increased by 84% from 1998 to 2003 and slightly increased by 10% from 2003 to 2008. The peak incidence rate during 1998 to 2008 in this population was 0.81 per 100,000 in 2007. From 1998 to 2008, the male to female ratio of new cases ranged from 1.25 to 2.18. The crude prevalence rate in 1998 and 2008 was 0.39 per 100,000 and 4.62 per 100,000, respectively. Over the 10-year period, the UC incidence and prevalence rates had an increasing trend in our populations.

The onset age (mean ± SD) of new UC cases was 45.08 ± 15.04 years on average during 1998 to 2008. The onset age was stable with each year, with the lowest ranging from 42.76 ± 15.09 years in 2005 to the highest ranging from 46.97 ± 15.77 years in 2000. The onset age for females (46.21 ± 13.1 years) was slightly more than that for males (44.42 ± 15.08 years) on average during 1998 to 2008 (Table 2). On the onset age distribution of UC, the disease onset of UC was found to range from children to elderly and predominant at the 30 to 49 years age group for both males and females. The peak age-specific incidence and prevalence of UC was in the 50 to 59 years age group (Table 3). The age of patients with UC showed a stable trend during 1998 to 2008 (Table 4). However, the age gap between the most young and the most old had sustained, rising over the past decade for both males and females.

Table 1 – Incidence and prevalence of ulcerative colitis* in Taiwan, 1998–2008.

Year	New cases			Incidence					Total cases			Prevalence				
	T	M	F	T1	T2	M	F	M/F	T	M	F	T1	T2	M	F	M/F
1998	81	45	36	0.37	0.38	0.40	0.34	1.25	85	49	36	0.39	0.39	0.44	0.34	1.36
1999	114	77	37	0.52	0.53	0.68	0.35	2.03	181	110	71	0.82	0.83	0.97	0.67	1.53
2000	93	62	31	0.43	0.43	0.56	0.28	2.06	245	156	89	1.11	1.11	1.39	0.82	1.78
2001	105	72	33	0.47	0.46	0.63	0.30	2.18	320	207	113	1.44	1.42	1.83	1.03	1.85
2002	148	91	57	0.66	0.64	0.79	0.52	1.60	434	274	160	1.94	1.89	2.40	1.45	1.73
2003	153	95	58	0.68	0.66	0.83	0.52	1.66	525	328	197	2.33	2.24	2.86	1.78	1.67
2004	131	81	50	0.58	0.54	0.70	0.46	1.59	574	361	213	2.54	2.4	3.14	1.92	1.69
2005	147	94	53	0.65	0.62	0.81	0.47	1.77	654	414	240	2.87	2.67	3.58	2.14	1.73
2006	182	107	75	0.79	0.75	0.91	0.66	1.41	807	499	308	3.52	3.26	4.30	2.73	1.62
2007	186	114	72	0.81	0.74	0.99	0.63	1.60	955	594	361	4.16	3.71	5.12	3.18	1.65
2008	182	107	75	0.78	0.72	0.91	0.65	1.43	1087	673	414	4.62	4.11	5.67	3.55	1.63

F, female; ICD, International Classification of Diseases; M, male; M/F, male-to-female ratio; T, total.
T1, crude rate.
T2, age-standardized rate, 2000 population in Taiwan as standard population.
* Series accidents and disease of *ICD*: 556.

Table 2 – Onset age of ulcerative colitis* in Taiwan, 1998–2008.

Year	New cases				Males				Females			
	N	Mean ± SD	Min	Max	N	Mean ± SD	Min	Max	N	Mean ± SD	Min	Max
1998	81	46.20 ± 15.19	16.25	76.42	45	46.21 ± 15.73	20.70	76.42	36	46.17 ± 14.70	16.25	72.88
1999	114	46.21 ± 14.54	11.95	80.01	77	45.88 ± 15.01	11.95	78.18	37	46.90 ± 13.69	20.83	80.01
2000	93	44.31 ± 14.99	4.25	83.59	62	44.43 ± 13.65	20.27	83.59	31	44.08 ± 17.61	4.25	74.72
2001	105	44.99 ± 14.24	15.29	76.41	72	43.83 ± 15.02	15.89	76.41	33	47.52 ± 12.20	15.29	74.73
2002	148	44.75 ± 14.22	3.03	79.45	91	43.03 ± 14.56	3.03	77.37	57	47.48 ± 13.33	26.51	79.45
2003	153	46.97 ± 15.77	15.64	80.72	95	45.85 ± 16.05	16.47	80.72	58	48.80 ± 15.26	15.64	76.97
2004	131	46.76 ± 14.67	13.80	86.41	81	46.77 ± 13.92	13.80	86.41	50	46.75 ± 15.96	17.19	80.96
2005	147	42.76 ± 15.09	11.93	86.03	94	42.31 ± 14.31	15.90	86.03	53	43.57 ± 16.49	11.93	73.29
2006	182	43.67 ± 16.52	9.62	90.26	107	43.42 ± 17.10	9.62	90.26	75	44.03 ± 15.75	11.00	82.84
2007	186	46.03 ± 15.57	2.94	82.37	114	44.35 ± 15.46	15.18	82.37	72	48.70 ± 15.48	2.94	79.20
2008	182	43.24 ± 14.66	1.71	86.64	107	42.50 ± 15.10	1.71	86.64	75	44.30 ± 14.05	12.23	81.82

ICD, International Classification of Diseases.
* Series accidents and disease of *ICD*:556.

Table 3 – Age distribution of ulcerative colitis* in Taiwan, 1998–2008.

Age group (y)	New cases			Incidence				Total cases			Prevalence			
	T	M	F	T	M	F	M/F	T	M	F	T	M	F	M/F
<20	51	32	19	0.08	0.09	0.06	1.68	137	71	66	0.2	0.2	0.20	1.08
20–29	203	148	55	0.49	0.70	0.27	2.69	567	411	156	1.36	1.93	0.76	2.63
30–39	360	222	138	0.87	1.06	0.68	1.61	1229	812	417	2.98	3.89	2.05	1.95
40–49	359	223	136	0.90	1.11	0.69	1.64	1526	973	553	3.85	4.86	2.81	1.76
50–59	295	175	120	1.13	1.34	0.91	1.46	1233	735	498	4.71	5.63	3.79	1.48
60–69	155	86	69	0.95	1.08	0.83	1.25	689	388	301	4.23	4.88	3.61	1.29
70+	99	59	40	0.64	0.74	0.54	1.48	486	275	211	3.15	3.44	2.83	1.30

F, female; *ICD, International Classification of Diseases*; M, male; M/F, male-to-female ratio; T, total.
* Series accidents and disease of *ICD*: 556.

In our survey, associated diseases in patients with UC included irritable bowel syndrome (26.87%), other unspecified noninfectious gastroenteritis and colitis (22.74%), and hemorrhoids (21.88%). More than 70% of the patients had a concomitant diagnosis of gastrointestinally relevant diseases about symptoms and signs of UC (Table 5). Among 1522 patients with UC, comorbidities about the ventilatory diseases included acute nasopharyngitis (6.64%) and upper respiratory tract infections (14.91%). The chronic diseases noted were hepatitis (7.36%), diabetes (6.64%), and hypertension (7.69%). Anemia complication was seen in 9.9% (n = 152) of the cases.

Based on medical expenditure data, four medical categories treated in outpatients with UC increased in number of patients and medical expenditure with time from 1998 to 2008 (Table 6). By comparing with outpatients, the proportion of each medical category usage and medical expenditure for inpatients remained steady and varied from year to year. Among the four medical categories, mesalamine accounted for the largest proportion of medical users. The average proportion of mesalamine users to total cases was 74%, and the proportion in each year remained stable from 1998 to 2008. In our survey, the average proportions of sulfasalazine and corticosteroid users to total cases were 20% and 31%, respectively. Despite the fact that the number of immunosuppressant agent users within the four medical categories in outpatients and inpatients accounted for the lowest in each year, the total immunosuppressant agent expenditure still remained second highest within the four medical categories after 2004. The highest proportion of immunosuppressant agent users to total cases was in 2008 at 7% and the lowest in 1998 at 0%, with the number of drug users increasing twofold from 2006 to 2008.

The average medical expenditure per patient with UC was 13,964 NTD, representing 1.7-fold to the average medical expenditure per each Taiwan population member in 2008 (Table 7). Furthermore, despite an increase in the total cases and medical users with time in our survey, the average medical expenditure of patients with UC remained decreasing and the proportion of average medical expenditure in patients with UC to that in the general population also decreased with time from 2001 to 2008.

Discussion

UC has been widely discussed in Western countries and been considered as a rare disease among Asian countries [2,6,8,38]. In the past two decades, a number of articles have shown a rising trend in the prevalence and incidence of UC in Asian countries, especially in East Asian countries (Table 8) [1,3–5,39–46]. In our study, the incidence rate (0.38–0.72 per 100,000) in Taiwan is similar to that in Hong Kong (0.40 per 100,000) [1], but lower than that in India (6.02 per 100,000) [45] and Lebanon (4.1 per 100,000) [42]. Furthermore, the trend of age-adjusted incidence rate observed across the entire time frame appeared as a rising trend in the Taiwan population. Our present study is consistent with South Korean studies, which found a sustained rising trend of UC

Table 4 – Prevalence age of ulcerative colitis* in Taiwan, 1998–2008.

Year	Total cases				Males				Females			
	N	Mean ± SD	Min	Max	N	Mean ± SD	Min	Max	N	Mean ± SD	Min	Max
1998	85	46.33 ± 15.08	16.25	76.42	49	46.45 ± 15.50	20.70	76.42	36	46.17 ± 14.70	16.25	72.88
1999	181	46.07 ± 14.56	11.95	80.01	110	45.72 ± 14.98	11.95	78.18	71	46.61 ± 13.96	16.76	80.01
2000	245	46.25 ± 14.50	4.25	83.59	156	45.52 ± 14.19	19.75	83.59	89	47.53 ± 15.02	4.25	76.65
2001	320	46.34 ± 14.56	4.65	84.12	207	45.55 ± 14.42	15.89	84.12	113	47.78 ± 14.77	4.65	77.60
2002	434	46.46 ± 14.48	3.03	84.79	274	45.20 ± 14.50	3.03	84.79	160	48.62 ± 14.23	5.70	79.45
2003	525	47.49 ± 14.89	3.81	83.46	328	46.32 ± 14.99	3.81	83.46	197	49.44 ± 14.56	6.68	79.74
2004	574	47.95 ± 14.41	4.74	86.41	361	46.98 ± 13.97	4.74	86.41	213	49.60 ± 15.02	7.72	80.96
2005	654	47.76 ± 14.65	5.68	86.62	414	46.44 ± 14.04	5.68	86.03	240	50.03 ± 15.41	9.18	86.62
2006	807	47.37 ± 15.01	6.74	90.26	499	46.82 ± 14.85	6.74	90.26	308	48.25 ± 15.26	9.63	82.84
2007	955	47.56 ± 14.99	2.94	91.23	594	46.89 ± 14.83	8.18	91.23	361	48.66 ± 15.22	2.94	83.52
2008	1087	47.37 ± 15.04	1.71	91.52	673	46.69 ± 14.89	1.71	91.52	414	48.48 ± 15.23	3.68	82.17

ICD, International Classification of Diseases.
* Series accidents and disease of *ICD*: 556.

Table 5 – The top 20 coexisting diseases of patients with ulcerative colitis* at onset of ulcerative colitis in Taiwan, 1998–2008 (N = 1522).

ICD-9	Frequency	%	Disease name
564.1	409	26.87	Irritable bowel syndrome
558.9	333	21.88	Other and unspecified noninfectious gastroenteritis and colitis
465.9	227	14.91	Acute upper respiratory infections of unspecified site
536.9	217	14.26	Unspecified functional disorder of stomach
455.6	203	13.34	Unspecified hemorrhoids without mention of complication
789	184	12.09	Other symptoms involving abdomen and pelvis
533.9	175	11.50	Peptic ulcer, site unspecified, unspecified as acute or chronic, without mention of hemorrhage or perforation
564.9	172	11.30	Unspecified functional disorder of intestine
285.9	152	9.99	Anemia, unspecified
578.9	147	9.66	Hemorrhage of gastrointestinal tract, unspecified
455	143	9.40	Hemorrhoids
564	129	8.48	Functional digestive disorders, not elsewhere classified
555.1	125	8.21	Regional enteritis, large intestine
536.8	124	8.15	Dyspepsia and other specified disorders of function of stomach
455.8	119	7.82	Unspecified hemorrhoids with other complication
401.9	117	7.69	Essential hypertension, unspecified
571.4	112	7.36	Chronic hepatitis
300	106	6.96	Neurotic disorders
250	101	6.64	Diabetes mellitus
460	101	6.64	Acute nasopharyngitis (common cold)

ICD-9, International Classification of Diseases, Ninth Revision.
* Series accidents and disease of *ICD*:556.

incidence rates in the recent 10-year period [5]. Moreover, the adjusted prevalence rates (3.26 per 100,000) in 2006 are lower than those in other East Asian countries, such as Hong Kong (6.99 per 100,000) [1], Japan (63.6 per 100,000) [3], and South Korea (30.9 per 100,000) [5]. The reason of lower prevalence rates in our population may come from the CI certificate needing strict evaluation by two specialty physicians in the Department of Health, which leads to the actual number of cases being underestimated. Also, accurate case numbers may be underestimated owing to patients who died before they could apply for a CI certificate and owing to patients who did not apply for a CI certificate. However, the rising trend of prevalence rates in our findings is also consistent with other recent studies.

Our study findings were consistent with most studies that the male is the predominant gender (M/F = 1.25:1–2.5:1) in patients with UC [3,18,19]. Furthermore, the onset age of new UC cases was 45.08 years and the predominant age range was 30 to 49 years, which is similar as in other studies in Asia [3,21]. In contrast to other studies, our data showed that the peak age-specific incidence and prevalence rates were in the 50 to 59 years age group.

The signs and symptoms of UC patients can be associated with different gastrointestinal signs and symptoms, and local or extraintestinal complications with no treatment patients. In our findings, more than 70% of coexisting diseases in patients with UC were signs and symptoms of UC. Local complications, such as massive hemorrhage, intestinal perforation or stricture, and colon cancer, would occur in a number of patients with UC [30,47,48]. CRC is a serious complication in patients with UC, and a number of studies showed that Asian patients have lower incidence rates (0%–1.8%) than do Western patients (3%–5%) [47]. Despite this, we did not find CRC in the top 20 coexisting diseases from our results; 10-year CRC prevalence still observed a rate of 4.99% for colon cancer and 0.59% for rectum and anal canal cancer. Moreover, a lower CRC risk was observed for Asian patients with UC from current studies, but more studies need to be performed for CRC surveillance in Asian patients with UC. In our results, anemia had a high disease prevalence (9.99%) in our population from our database. Similarly, a number of studies indicated that anemia is a common complication in patients with UC and the mechanism of anemia with UC diseases may be due to gastrointestinal bleeding, poor absorption, iron deficiency, and disease severity [29]. Some recent studies showed that chronic diseases, including hypertension and metabolic syndrome, were a common condition within patients with UC [21,49]. Our findings are consistent with other studies that diabetes (6.64%) and hypertension (7.69%) are observed in the top 20 coexisting diseases with UC.

No recent studies have reported the medical expenditure and use trend of patients with UC in Asian countries. Therefore, our study represents an important contribution to the current literature describing the medical burden of patients with UC. From the results, we see that for four medical categories (mesalamine, sulfasalazine, corticosteroids, and immunosuppressant agents) used for the treatment of patients with UC, medical users and expenditure increased across time from 1998 to 2008. Comparing inpatient with outpatient episodes, we see that there was a lower proportion of each medical category usage and expenditure at the inpatient level and the proportion of inpatients using the medicines remained steady with time. Between years 1998 and 2008, the proportion of different categories of medical users to total cases had the same trend in mesalamine (72%–76%), sulfasalazine (20%–27%), and corticosteroids (30%–35%), but a rising trend in immunosuppressant agent users from 0% in 1998 to 7% in 2008. In addition, it was evident from the study that the number of patients prescribed immunosuppressant agents had the lowest drug expenditure and average drug expenditure from 2001 to 2008 remained second highest. This signified the urgency in discussing pharmacoeconomic strategies of immunosuppressant agent treatment in patients with UC. In our survey, the average medical expenditure of patients with UC remained decreasing from 2001 to 2008, and the proportion of

Table 6 – Each drug's utilization and expenditure in outpatient, inpatient, and total cases of patients with ulcerative colitis in Taiwan, 1998–2008.

Drug	Year	Outpatient		Inpatient		Total		
		No. of patients for whom prescribed	Total drug expenditure (NTD)	No. of patients for whom prescribed	Total drug expenditure (NTD)	No. of patients for whom prescribed	% to total	Average drug expenditure (NTD)
Mesalamine	1998	55	630,849	11	38,304	61	72	10,970
	1999	128	3,382,937	24	141,215	137	76	25,724
	2000	171	3,743,754	26	125,202	182	74	21,258
	2001	229	5,022,899	32	181,330	238	74	21,867
	2002	313	5,008,396	38	125,719	323	74	15,895
	2003	377	6,125,535	54	177,698	392	75	16,080
	2004	406	6,409,686	49	184,954	417	73	15,814
	2005	456	7,959,271	52	185,239	468	72	17,403
	2006	586	8,970,021	71	179,897	597	74	15,326
	2007	702	10,293,105	73	204,552	708	74	14,827
	2008	818	11,777,123	89	239,629	822	76	14,619
Sulfasalazine	1998	14	32,202	6	3,931	19	22	1,902
	1999	32	107,965	8	7,657	39	22	2,965
	2000	46	213,375	9	9,752	49	20	4,554
	2001	67	359,286	9	6,933	71	22	5,158
	2002	95	501,087	13	11,646	103	24	4,978
	2003	124	557,645	21	13,996	136	26	4,203
	2004	146	620,250	21	12,287	153	27	4,134
	2005	150	685,829	23	11,408	158	24	4,413
	2006	162	688,628	22	13,345	165	20	4,254
	2007	173	609,232	19	9,423	177	19	3,495
	2008	188	579,527	19	5,945	193	18	3,034
Corticosteroids	1998	10	2214	11	603	18	21	157
	1999	49	12,650	20	1,227	60	33	231
	2000	69	18,343	31	1,677	86	35	233
	2001	90	36,935	30	7,886	100	31	448
	2002	122	54,015	37	8,330	133	31	469
	2003	141	45,292	50	3,602	164	31	298
	2004	165	46,767	50	4,150	174	30	293
	2005	192	53,724	51	4,851	204	31	287
	2006	245	56,791	64	3,266	255	32	236
	2007	286	79,152	66	6,028	293	31	291
	2008	344	94,158	84	7,138	353	32	287
Immunosuppressant agents	1998	0	0	0	0	0	0	0
	1999	1	902	0	0	1	1	902
	2000	2	1,578	1	773	3	1	784
	2001	4	21,556	3	2,963	5	2	4,904
	2002	7	29,086	3	2,175	7	2	4,466
	2003	13	42,175	3	3,748	14	3	3,280
	2004	15	84,591	6	6,264	19	3	4,782
	2005	21	125,674	5	17,155	21	3	6,801
	2006	32	166,919	5	7,352	33	4	5,281
	2007	43	368,404	11	32,002	47	5	8,519
	2008	69	571,451	18	18,341	72	7	8,192

Table 7 – Medical expenditure of ulcerative colitis compared with general population medical expenditure in Taiwan, 1998–2008.

Year	Total cases	No. of patients for medication	No. of patients for medical service	All medical service expenditures (NTD)	Average medical expenditure per patient (NTD)	Average medical expenditure per each Taiwan population member (NTD)	Average medical expenditure fold to general population
1998	85	76	303	712,283	9,372	5,003	1.9
1999	181	160	1,604	3,654,553	22,841	5,537	4.1
2000	245	208	2,142	4,117,975	19,798	5,857	3.4
2001	320	280	3,112	5,640,673	20,145	5,875	3.4
2002	434	383	3,902	5,742,119	14,992	6,117	2.5
2003	525	469	4,427	6,970,943	14,863	6,592	2.3
2004	574	513	5,049	7,405,209	14,435	7,126	2.0
2005	654	575	6,286	9,094,475	15,816	7,199	2.2
2006	807	713	7,669	10,150,886	14,237	7,495	1.9
2007	955	832	9,342	11,706,148	14,070	7,970	1.8
2008	1,087	957	10,995	13,363,700	13,964	8,196	1.7

average medical expenditure in patients with UC to that in the general population also decreased with time. The reason of the decreasing tread may be fluctuations in medical payment prices and health care policies. There are limited data on the correlation between medical trends of patients with UC and health care policy, but it may be prudent to monitor patients with UC for disease burden after UC diagnosis.

This study had the largest sample and the longest study period for the estimation of incidence and prevalence rates of UC in Taiwan. Although a number of studies have been conducted in Asians, they still lack epidemiology information and study in our population. We conducted the study by using the NHIRD. This database is from one single-payer National Health Insurance program that enrolled 98% of Taiwan's population. This database includes complete Taiwan population medical records. In our study, we ascertained UC cases from CI certificates, which are evaluated by two specialty physicians, which decreases the problem of diagnostic accuracy. There are, however, some limitations in the present study. First, UC patients applying for CI certificates were selected on the basis of their first claim date; therefore, a time delay may be present in this study. Unfortunately, the database used in our study was a de-identified secondary database. Therefore, it is difficult to determine whether underestimation occurred. Second, information on personal habits such as smoking, lifestyle, body weight, and disease severity was not available from the NHIRD. Some articles have discussed the disease severity condition and clinical characteristics of UC are different in Asian and Western populations. In the present study, we were unable to evaluate the severity in other countries and compare the severity of associated signs and symptoms with data from other countries or populations. Third, we had no imaging findings or data of patients with UC, and these might be potential confounders. Last, the health care policy, area of residence, individual countries, and socioeconomic status were still not included in our outcome.

In conclusion, UC in Taiwan still presents a rare disease than in Western countries. However, the rising trend of incidence and prevalence rates in Asian countries has been discussed and observed in the past decade. In Taiwanese population, UC also had a definite rising trend in prevalence and incidence rates from 1998 to 2008. The epidemiological results were similar to those in some East Asian countries but different from those in Western and West Asian countries. More than 70% of the patients with UC were using mesalamine in Taiwan, but the mesalamine expenditure also kept on increasing each year. Immunosuppressant

Table 8 – Updated epidemiology studies of ulcerative colitis in Asians.

Area	Country	Study period	Incidence per million per year	Prevalence per million
East Asian	Taiwan (present study)	1998–2008	0.78	4.62
	Japan [4]	1991	1.95	18.1
	Japan [3]	2005	–	63.6
	Hong Kong [1]	1997–2006	0.4	6.99
	Hong Kong [39]	2001	1.2	–
	Hong Kong [40]	2006	2.1	26.5
	South Korea [5]	1986–2005	3.08	30.87
South-East Asian	Singapore [41]	2004	–	6.0
West Asian	Lebanon [42]	2000–2004	4.1	106.2
	Kuwait [43]	1985–1999	2.80	41.7
	Israel, Kibbutz [44]	1987–1997	5.04	167.2
South Asian	North India, Punjab [45]	1999–2000	6.02	44.3
	Sri Lanka [46]	2007–2008	0.69	5.3

agents had the lowest users and the second highest medical expenditure. Decreasing medical expenditure trends in patients with UC were observed after 2001. In the future, the UC patient survey outcomes, clinical features, and medical treatment need to be explored in our population to help clinical services and treatment becoming more better and approaching perfection day by day.

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REFERENCES

[1] Lok KH, Hung HG, Ng CH, et al. Epidemiology and clinical characteristics of ulcerative colitis in Chinese population: experience from a single center in Hong Kong. J Gastroenterol Hepatol 2008;23:406–10.
[2] Thia KT, Loftus EV Jr, Sandborn WJ, Yang SK. An update on the epidemiology of inflammatory bowel disease in Asia. Am J Gastroenterol 2008;103:3167–82.
[3] Asakura K, Nishiwaki Y, Inoue N, et al. Prevalence of ulcerative colitis and Crohn's disease in Japan. J Gastroenterol 2009;44:659–65.
[4] Morita N, Toki S, Hirohashi T, et al. Incidence and prevalence of inflammatory bowel disease in Japan: nationwide epidemiological survey during the year 1991. J Gastroenterol 1995;30(Suppl. 8):1–4.
[5] Yang SK, Yun S, Kim JH, et al. Epidemiology of inflammatory bowel disease in the Songpa-Kangdong district, Seoul, Korea, 1986–2005: a KASID study. Inflamm Bowel Dis 2008;14:542–9.
[6] Hou JK, El-Serag H, Thirumurthi S. Distribution and manifestations of inflammatory bowel disease in Asians, Hispanics, and African Americans: a systematic review. Am J Gastroenterol 2009;104:2100–9.
[7] Ooi CJ, Fock KM, Makharia GK, et al. The Asia-Pacific consensus on ulcerative colitis. J Gastroenterol Hepatol 2010;25:453–68.
[8] Goh K, Xiao SD. Inflammatory bowel disease: a survey of the epidemiology in Asia. J Dig Dis 2009;10:1–6.
[9] Mahid SS, Minor KS, Soto RE, et al. Smoking and inflammatory bowel disease: a meta-analysis. Mayo Clin Proc 2006;81:1462–71.
[10] Jones DT, Osterman MT, Bewtra M, Lewis JD. Passive smoking and inflammatory bowel disease: a meta-analysis. Am J Gastroenterol 2008;103:2382–93.
[11] Lakatos PL. Environmental factors affecting inflammatory bowel disease: have we made progress? Dig Dis 2009;27:215–25.
[12] Machida H, Tsukamoto K, Wen CY, et al. Association of polymorphic alleles of CTLA4 with inflammatory bowel disease in the Japanese. World J Gastroenterol 2005;11:4188–93.
[13] Myung SJ, Yang SK, Jung HY, et al. HLA-DRB1*1502 confers susceptibility to ulcerative colitis, but is negatively associated with its intractability: a Korean study. Int J Colorectal Dis 2002;17:233–7.
[14] Gulwani-Akolkar B, Akolkar PN, Lin XY, et al. HLA class II alleles associated with susceptibility and resistance to Crohn's disease in the Jewish population. Inflamm Bowel Dis 2000;6:71–6.
[15] Yoshitake S, Kimura A, Okada M, et al. HLA class II alleles in Japanese patients with inflammatory bowel disease. Tissue Antigens 1999; 53(4, Pt 1):350–8.
[16] Shen XY, Shi RH, Wang Y, et al. Toll-like receptor gene polymorphisms and susceptibility to inflammatory bowel disease in Chinese Han and Caucasian populations. Zhonghua Yi Xue Za Zhi 2010;90:1416–20.
[17] Flasar MH, Cross RK, Doman DB. Current and future role of serogenomics in ulcerative colitis. Gastroenterol Hepatol (N Y) 2011;7:720–7.
[18] Yoshida Y, Murata Y. Inflammatory bowel disease in Japan: studies of epidemiology and etiopathogenesis. Med Clin North Am 1990;74:67–90.
[19] Yang SK, Hong WS, Min YI, et al. Incidence and prevalence of ulcerative colitis in the Songpa-Kangdong District, Seoul, Korea, 1986–1997. J Gastroenterol Hepatol 2000;15:1037–42.
[20] Wei SC, Shieh MJ, Chang MC, et al. Long-term follow-up of ulcerative colitis in Taiwan. J Chin Med Assoc 2012;75:151–5.
[21] Lin HC, Chiu CC, Chen SF, et al. Ulcerative colitis and pregnancy outcomes in an Asian population. Am J Gastroenterol 2010;105:387–94.
[22] Tsai CH, Chen HL, Ni YH, et al. Characteristics and trends in incidence of inflammatory bowel disease in Taiwanese children. J Formos Med Assoc 2004;103:685–91.
[23] Chang LM, Ho KS, Chen GH. Ulcerative colitis in Taichung Veterans General Hospital: a clinical study. Gaoxiong Yi Xue Ke Xue Za Zhi 1995;11:641–9.
[24] Sonnenberg A. Time trends of mortality from Crohn's disease and ulcerative colitis. Int J Epidemiol 2007;36:890–9.
[25] Ouyang Q, Tandon R, Goh KL, et al. The emergence of inflammatory bowel disease in the Asian Pacific region. Curr Opin Gastroenterol 2005;21:408–13.
[26] Jiang XL, Cui HF. An analysis of 10218 ulcerative colitis cases in China. World J Gastroenterol 2002;8:158–61.
[27] Langan RC, Gotsch PB, Krafczyk MA, Skillinge DD. Ulcerative colitis: diagnosis and treatment. Am Fam Phys 2007;76:1323–30.
[28] Kornbluth A, Sachar DB. Ulcerative colitis practice guidelines in adults (update): American College of Gastroenterology, Practice Parameters Committee. Am J Gastroenterol 2004;99:1371–85.
[29] Gisbert JP, Gomollon F. Common misconceptions in the diagnosis and management of anemia in inflammatory bowel disease. Am J Gastroenterol 2008;103:1299–307.
[30] Danovitch SH. Fulminant colitis and toxic megacolon. Gastroenterol Clin North Am 1989;18:73–82.
[31] Bernstein CN, Wajda A, Blanchard JF. The incidence of arterial thromboembolic diseases in inflammatory bowel disease: a population-based study. Clin Gastroenterol Hepatol 2008;6:41–5.
[32] Bernstein CN, Blanchard JF, Rawsthorne P, Yu N. The prevalence of extraintestinal diseases in inflammatory bowel disease: a population-based study. Am J Gastroenterol 2001;96:1116–22.
[33] Palm O, Moum B, Jahnsen J, Gran JT. The prevalence and incidence of peripheral arthritis in patients with inflammatory bowel disease, a prospective population-based study (the IBSEN study). Rheumatology (Oxford) 2001;40:1256–61.
[34] Irvine EJ. Quality of life of patients with ulcerative colitis: past, present, and future. Inflamm Bowel Dis 2008;14:554–65.
[35] Longobardi T, Jacobs P, Wu L, Bernstein CN. Work losses related to inflammatory bowel disease in Canada: results from a National Population Health Survey. Am J Gastroenterol 2003;98:844–9.
[36] Longobardi T, Bernstein CN. Utilization of health-care resources by patients with IBD in Manitoba: a profile of time since diagnosis. Am J Gastroenterol 2007;102:1683–91.
[37] Kappelman MD, Rifas-Shiman SL, Porter CQ, et al. Direct health care costs of Crohn's disease and ulcerative colitis in US children and adults. Gastroenterology 2008;135:1907–13.
[38] Baumgart DC, Carding SR. Inflammatory bowel disease: cause and immunobiology. Lancet 2007;369:1627–40.
[39] Leong RW, Lau JY, Sung JJ. The epidemiology and phenotype of Crohn's disease in the Chinese population. Inflamm Bowel Dis 2004;10:646–51.
[40] Chow DK, Leong RW, Tsoi KK, et al. Long-term follow-up of ulcerative colitis in the Chinese population. Am J Gastroenterol 2009;104:647–54.
[41] Lee YM, Fock K, See SJ, et al. Racial differences in the prevalence of ulcerative colitis and Crohn's disease in Singapore. J Gastroenterol Hepatol 2000;15:622–5.
[42] Abdul-Baki H, ElHajj I, El-Zahabi LM, et al. Clinical epidemiology of inflammatory bowel disease in Lebanon. Inflamm Bowel Dis 2007;13:475–80.
[43] Al-Shamali MA, Kalaoui M, Patty I, et al. Ulcerative colitis in Kuwait: a review of 90 cases. Digestion 2003;67:218–24.
[44] Niv Y, Abuksis G, Fraser GM. Epidemiology of ulcerative colitis in Israel: a survey of Israeli kibbutz settlements. Am J Gastroenterol 2000;95:693–8.
[45] Sood A, Midha V, Sood N, et al. Incidence and prevalence of ulcerative colitis in Punjab, North India. Gut 2003;52:1587–90.
[46] Niriella MA, De Silva AP, Dayaratne AH, et al. Prevalence of inflammatory bowel disease in two districts of Sri Lanka: a hospital based survey. BMC Gastroenterol 2010;10:32.
[47] Kim BJ, Yang SK, Kim JS, et al. Trends of ulcerative colitis-associated colorectal cancer in Korea: a KASID study. J Gastroenterol Hepatol 2009;24:667–71.
[48] Eaden J, Abrams K, Ekbom A, et al. Colorectal cancer prevention in ulcerative colitis: a case-control study. Aliment Pharmacol Ther 2000;14:145–53.
[49] Yorulmaz E, Adali G, Yorulmaz H, et al. Metabolic syndrome frequency in inflammatory bowel diseases. Saudi J Gastroenterol 2011;17:376–82.